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Temperature-Controlled Laser Photocoagulation of Soft Tissue: In Vivo Evaluation Using a Tissue Welding Model

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Background and Objective: **Laser surgical procedures involving photocoagulation of soft tissue have relied on subjective visual endpoints. The thermal damage to the denatured tissue in these procedures is highly dependent on the tissue temperatures achieved during laser irradiation. Therefore, a system capable of real time temperature monitoring and closed loop feedback was used to provide temperature controlled photocoagulation (TCPC).**

Study Design/Materials and Methods: **The TCPC system consisted of a 1.32 μm Nd:YAG laser, an infrared thermometer, and a microprocessor for data acquisition and feedback control. A porcine skin model was used. Tissue welds were completed to evaluate the photocoagulation effects at different predetermined temperatures. A quantitative measurement of tissue photocoagulation was obtained by tensile strength measurements of the laser repairs. Histology of the irradiated tissue was used to determine the extent of thermal injury associated with different photocoagulation temperatures.**

Results: **The TCPC system was capable of maintaining a relatively constant temperature (±4°C) during laser irradiation. The tensile strengths of acute repairs increased with temperature over the range studied (65–95°C). Tensile measurements made after several days of healing showed that higher temperature (95°C) welds had lower strengths than repairs completed at lower (65°C or 75°C) temperatures and were significantly lower at 3 days. Acute histology showed that the amount thermal damage was strongly dependent on the tissue temperature and increased both in tissue depth and lateral to the repair with temperature. The histologic results suggest that the increase in the acute repair tensile strength as the weld temperature increased was due to an increase in the depth of tissue photocoagulation. The increase in the lateral tissue injury measured histologically for higher temperature welds likely resulted in the decreased chronic tensile strengths, as a healing response to excessive thermal damage.**

Conclusion: **Tissue temperatures can be controlled during laser photocoagulation of skin. The degree of acute and chronic tissue damage is highly dependent on the temperature during welding. By controlling the tissue temperature during laser procedures, the surgical outcome can be more reliably predicted and reproduced, as compared to the conventional open loop methods. In**

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addition, the use of a TCPC system should significantly reduce the learning curve for photothermal surgical procedures.

Key words: porcine, skin, solder, tensile strength, thermal denaturation

INTRODUCTION

Advanced systems are currently being evaluated for real time monitoring and control in medical procedures involving lasers [1]. These systems generally consist of a sensor, capable of rapidly measuring a tissue parameter of interest, coupled to a feedback loop that adjusts the laser power in response to the measurement. The response time of this type of system can be significantly quicker than the response time of the surgeon. These systems are useful for remote surgery performed endoscopically where visibility is restricted [2]. In addition, sensors can be used to monitor tissue parameters not visually discernible. One "invisible" tissue parameter being studied for feedback control is surface temperature [3].

Tissue temperature is extremely important for surgery involving laser induced photocoagulation. In these procedures, the laser is used strictly as a source of heat to cause thermal denaturation of the illuminated tissue proteins. Here, the laser energy deposited in the tissue is significantly below that needed for ablation (i.e. vaporization) of the tissue. This occurs when the laser energy being used is only weakly absorbed by the tissue, as is the case for soft tissue procedures using Nd:YAG lasers, which are the most common laser type currently in use. In the case of tissue photocoagulation, several variables can influence the clinical outcome. For instance, disparities in tissue properties can cause differences in the absorption characteristics. In addition, the fluence (Joules/cm^2) on the tissue can vary significantly for identical procedures, if the laser spot sizes or energy delivery rate is varied. These differences will cause the tissue temperature to fluctuate during laser procedures. Since the thermal damage to the irradiated tissue is strongly dependent on the elevated temperature achieved during the laser procedure, the resultant surgical outcome is highly variable. Temperature-controlled photocoagulation (TCPC) has been suggested as a means of normalizing these factors permitting a more reproducible laser procedure to be accomplished [1,4].

Laser photocoagulation procedures are currently performed with a human-based feedback system. Specifically, the surgeon uses visual cues to determine the extent of thermal damage to the laser-irradiated tissue. The linear delivery rate (i.e., the rate at which the surgeon moves the beam across the tissue) is controlled as a result of this visual feedback system. A typical endpoint for photocoagulation is the blanching of tissue, which occurs when soft tissue is heated above its denaturation temperature. This cue is not instantaneous at temperatures below 90°C but occurs after a time delay, which increases with decreasing temperature [5]. However, the temperature at which tissue damage is irreversible for "short" exposure times (1 second or longer) is ~60°C [6]. Thus any photocoagulation effect caused by heating tissue to temperatures between 60°C and 90°C are outside of the range of immediate visual detection by the surgeon [5]. Furthermore, visual control of photocoagulation at tissue temperatures above 90°C is likewise extremely difficult and can often lead to tissue charring, which can result in impaired healing at the repair site. Therefore, a system capable of TCPC would provide a significant improvement in the degree of control of many laser procedures.

This report describes the use of a TCPC system for photocoagulation of skin. A tissue welding model was chosen. This model is useful because the temperature dependence of thermal coagulation could be quantified via a tensile strength measurement of the laser-welded repair. In addition, acute and chronic histopathology were completed to determine the extent of thermal tissue damage at several different temperatures.

MATERIALS AND METHODS

Temperature-Controlled Photocoagulation System

An instrument was constructed to allow real time monitoring and control of tissue temperature during laser photocoagulation procedures. The system consists of three parts: (1) a 1.32 μm Nd:YAG laser (LaserScope, San Jose, CA) with fiberoptic power delivery to the tissue, (2) an infrared thermometer for tissue surface temperature measurements (ABIOMED R&D, Danvers, MA), and (3) a microprocessor based system for temperature data acquisition and real time laser

power control to maintain a constant surface temperature (ABIOMED R&D, Danvers, MA). The TCPC system included an audio alarm to indicate that the selected tissue temperature has been reached. Details of each of the system components are given below.

A flashlamp pumped 1.32 μm Nd:YAG laser was used. The system was a modified medical laser system, which normally operates on the 1.06 μm Nd:YAG laser line. This laser was chosen because the penetration depth of light at this wavelength, defined as the 1/e-fold absorption length (1.7 mm) [7], is comparable to the skin thickness for the porcine model chosen (~3 mm). By "matching" the absorption depth to the tissue thickness, the laser energy delivery should be optimized for tissue welding [8]. In addition, previous studies have demonstrated that this laser wavelength can be used for full thickness tissue welds in skin [9]. The laser was used in two different modes: (1) photocoagulation was completed at a set laser power (2 watts) while the tissue temperature was passively monitored; the laser was used in this manner to obtain "open loop" welding data, and (2) TCPC was accomplished by feedback to an analog control of the flashlamp current. This "closed loop" method adjusted the laser power to maintain a constant predetermined tissue temperature with the maximum power limited to 3 watts during the control. The laser light was delivered to the tissue via a 300 μm (core diameter) silica fiber.

The infrared thermometer was a direct viewing device, which monitored a 0.4 mm spot at the tissue surface in the laser heated region. Detailed specifications of this thermometer have been reported previously [10]. The viewing area was imaged onto a thermopile (Heimann GmbH Model TPS 434-T) using a ZnSe lens. The temperature was obtained from the measurement of blackbody emission over the infrared wavelength range of 8–13 μm. Since the penetration depth of radiation in the 8–13 μm range is very short (~10 μm), the infrared thermometer employed here only viewed the surface temperature of the tissue. The thermometer was calibrated using a resistively heated black plate (emissivity = 0.99 over the wavelength range sensed). The temperature of this plate was measured using a second calibrated infrared thermometer (Omega Instruments OS-88000-K-1200), which viewed the same region of the black plate. Using this setup, a calibration curve was obtained for the infrared thermometer, which provided a measurement accurate to ±1°C over a temperature range from 60°C to 100°C [10].

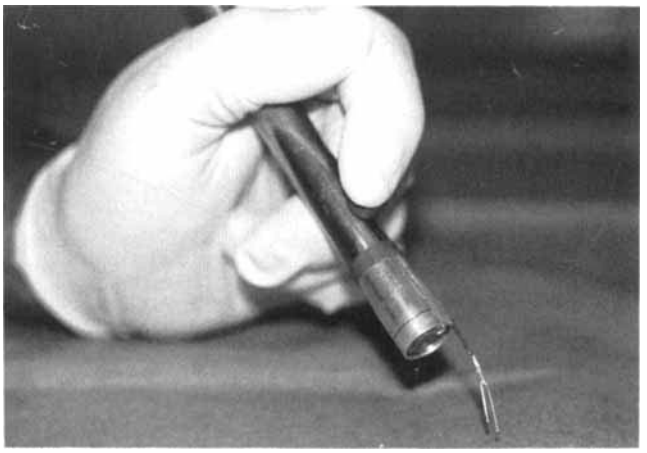

Fig. 1. Photograph of the surgical handpiece used in the in vivo studies. This handpiece incorporates an infrared thermometer, a laser delivery fiber, and a handswitch to activate the TCPC system.

The laser delivery fiber and the infrared thermometer were incorporated into a hand held surgical instrument (see this handpiece in Fig. 1). A stainless steel tube is used to direct the fiber to the weld region, and a wire lead attached to this tube is used to define the welding region and to provide tactile feedback for the surgeon. The infrared thermometer is enclosed in the body of the handle. This arrangement resulted in a 1.0 mm laser heated spot concentric with the 0.4 mm spot viewed by the thermometer. A switch to activate the laser was also incorporated in the handle. This handswitch design is similar to that used in conventional electrocautery devices.

The output from the infrared thermometer can be processed further using either a PC based system or a dedicated microprocessor for data acquisition and control. For the studies described below, a PC-based system was used with a data acquisition/control card and its corresponding software. This allowed easy storing and plotting of the resulting thermal profiles obtained while tissue welding. A simple feedback loop was used that changed the laser current every 16 ms, based on both the difference between the actual temperature and the desired temperature, and the difference in the actual temperatures for successive measurements. The laser control was accomplished via an analog input as described above.

Surgical Procedure

Four male Yucatan swine (12–15 kg) were used. The protocol employed was approved by the Institutional Animal Care and Use Committee.

Animals used in the study received humane care in compliance with the "Principles of Care and Use of Laboratory Animals" prepared by the National Academy of Sciences, published by the National Institute of Health (NIH Publication No. 80-23, revised 1985).

All animals were premedicated with Ketamine (20 mg/kg IM) followed by general anesthesia with Halothane by mask. Antibiotics (Bicillin) were administered preoperatively. All chronic procedures were completed in a sterile field. After the animals were prepped, thirty 2-cm-full thickness skin incisions were made on the dorsum of the pig with a #11 scalpel blade. Incisions were placed using a flexible plastic template to allow reproducible wounds to be made in each animal. Wounds were irrigated with 0.001% epinephrine to minimize bleeding. Once all incisions were made, the dorsal skin surface was cleaned using hydrogen peroxide to remove all dried blood. Incisions were closed using one of six repair techniques described below.

Laser-welded repairs were completed using either constant laser power (i.e., open loop) or the TCPC system. TCPC repairs were performed at 65°C, 75°C, 85°C, and 95°C. A single interrupted 5-0 prolene suture was placed in the center of all laser wounds to approximate the tissue edges during welding. Sutures were removed immediately following the laser procedure. In addition, a suture control group was repaired using two 5-0 prolene sutures evenly spaced across the wound. Three incisions were repaired for each of the six cases (open loop, 4 TCPC, and suture control).

A human albumin solder was used during all laser procedures. This solder consisted of a 50% concentration of human albumin (stock solution provided by the New York Blood Center, New York City). Details on the preparation of this solder have been previously described [11]. The albumin concentration was optimized to provide maximum strength for the laser repair [12]. In addition, the solder acts to fill small gaps between the tissue edges to ensure a continuous coagulation during welding, thereby resulting in a more homogeneous repair. Approximately 50 μl of solder was inserted between the tissue edges using a 22-gauge blunt tipped needle. Only a thin layer (<1 mm) of solder covered the surface of the tissue edges to be welded. Studies have demonstrated that the solder has low absorption at 1.32 μm; thus virtually all of the laser energy is absorbed by the underlying tissue (unpublished result).

Laser-welding procedures were completed under normal (i.e., unaided) viewing. Laser protective glasses were worn when the laser was active. The open loop welding was completed with a constant laser power. The visual cue monitored was tissue blanching during welding. For the TCPC laser repairs, the metal guide on the probe was placed against the tissue surface at one end of the repair. The laser/control system was activated via the handswitch, and the tissue temperature rose to the preset temperature while the surgeon held the probe in place. An audio alarm signaled the surgeon to hold the probe in place until the desired temperature was achieved. Once the tissue reached the desired temperature, the audio alarm ended, signaling the surgeon to advance the probe along the tissue surface. The laser power was automatically varied during the repair to maintain the desired surface tissue temperature. As stated above, the maximum power was limited to 3 watts during the TCPC procedure. This essentially limits the residence time for the irradiation of a given portion of the weld. For example, if the surgeon advanced the probe too rapidly, an audio alarm would indicate that the desired temperature was not achieved, at which time the surgeon would slow the speed of the closure. The total repair time was ~20 seconds for each 2-cm-long weld for both the open loop and TCPC laser repairs. Open loop and TCPC repairs were completed by a surgeon with substantial tissue welding experience (DPP) and a surgeon untrained (JMM) in tissue welding.

Following chronic laser welding procedures, the repairs were covered with a transparent sterile bandage (OpSite). Chronic wounds were evaluated at 3, 8, or 14 days following surgery. At the time of tissue harvest, the animals were anesthetized as described above. The dorsal skin was excised as a single flap, which included all of the repairs. The flap was placed on a moist towel to prevent desiccation prior to the tissue analysis. Animals were euthanized by intracardiac injection of Beuthanasia-D (0.1cc/kg).

Tissue Property Analysis

Analysis was completed on the fresh tissue within 2 hours of harvest. The tissue flap was divided to separate individual repairs and further bisected perpendicular to the repair. This resulted in six tissue sections for each of the different repair types. Five of these specimens were tested for tensile strength. The sixth specimen was fixed in 10% buffered formalin for histological analysis.

The tensile strength measurements were

performed with a commercial tensiometer (Instron Corp., Model Mini 55, Canton, MA). All tissue specimens tested were trimmed to conform to a 1 cm wide by 4 cm long template. Excess subcutaneous tissue was sharply removed leaving only the dermis and epidermis. The average thickness of the resulting tissue samples was 3.5 mm; however, the thickness of each specimen varied depending on the animal's age and the dorsal position of the original incision. In order to calculate the area of each wound being stressed, the thickness of each wound was measured. The tissue specimen was stressed to failure at a rate of 20 mm/min to determine the strength at the repair site. For the suture controls, the sutures were removed prior to tensile strength measurement. The maximum stress (in kiloPascals) needed to break the 1 cm wide repair was calculated by a software program supplied with the tensiometer.

Laser-welded tissue specimens underwent histological analysis to determine the zone of thermal injury. The samples were paraffin embedded and sectioned perpendicularly to the repair site in 7-μm-thick slices. Tissues were stained using both hematoxylin and eosin (H & E) and Masson's Trichrome.

RESULTS

In Vivo Temperature Measurement

The performance of the TCPC system was evaluated for open and closed loop tissue welding. The temperatures obtained during open loop repairs were monitored by the infrared thermometer. A limited number of skin incisions were also repaired using the closed loop control system described above operating between 65°C and 95°C. Results were obtained for a surgeon experienced in tissue welding techniques ("specialist"-DPP) and a surgeon untrained in tissue welding procedures ("novice"-JMM).

The temperature profiles achieved for four different cases of tissue welding are given in Figure 2. The open loop temperature profile obtained by the novice varied randomly between 70°C and 110°C. Since a constant power was used *and* the fluence was maintained by fixing the distance to the tissue via the guide on the handle (see Fig. 1), the differences in tissue temperature are primarily caused by changes in the speed at which the surgeon moves the beam across the tissue. The expert's open loop temperature profile obtained during welding, however, shows a repetitive variation of temperature between 70°C and 100°C. The visual control mechanism is demonstrated in Figure 2, as the surgeon cues on visible blanching of the tissue at ~90°C. In this case the surgeon "controls" the welding process by keeping the laser beam on a specific tissue spot until visual denaturation occurs, at which time the beam is manually redirected to adjacent tissue, which is at a lower temperature. The surgeon then looks for the visual cue before advancing the beam again.

The closed loop temperature profiles for tissue welding are given in Figure 2. Successful closed loop tissue welding depends on the ability to follow the audio cue for when the desired temperature has been reached and to move the laser beam in a controlled fashion. This motion is similar to other surgical procedures; therefore, little additional training is necessary for TCPC tissue welds. Graphs demonstrating these observations are shown in Figure 2, where the closed loop temperature profile obtained by the novice is not significantly different (after only a few minutes of training) than that achieved by the specialist.

Tensile Strength Measurement

Tensile strengths of the repairs were measured acutely, and at 3, 8, or 14 days. The weld strength was used as a method to quantitate the amount of photocoagulation at four different temperatures (65°C, 75°C, 85°C, and 95°C). The temperature range was chosen based on the temperatures measured for the open loop specialist welds in the studies given above. In addition, the lower temperature chosen (<65°C) was approximately the minimum weld temperature at which relatively robust welds could be obtained (i.e., repairs completed at lower set temperatures were generally too fragile to manipulate for the tensile strength measurements). At temperatures higher than the maximum temperature studied (>95°C), extreme visible thermal damage including ablation was noted. Since this latter process creates a tissue defect at the repair, a favorable outcome is not expected for tissue welding at these temperatures.

The results of the tensile strength measurements are given in Figure 3. The acute tensile strength increased with temperature over the range studied. The weld strengths at 95°C were significantly greater than the strengths obtained for repairs made at 65°C ($P < 0.01$) or 75°C ($P < 0.05$). The acute repair made at 85°C was also significantly stronger than the 65°C weld. The chronic data given in Figure 3 shows that the ten-

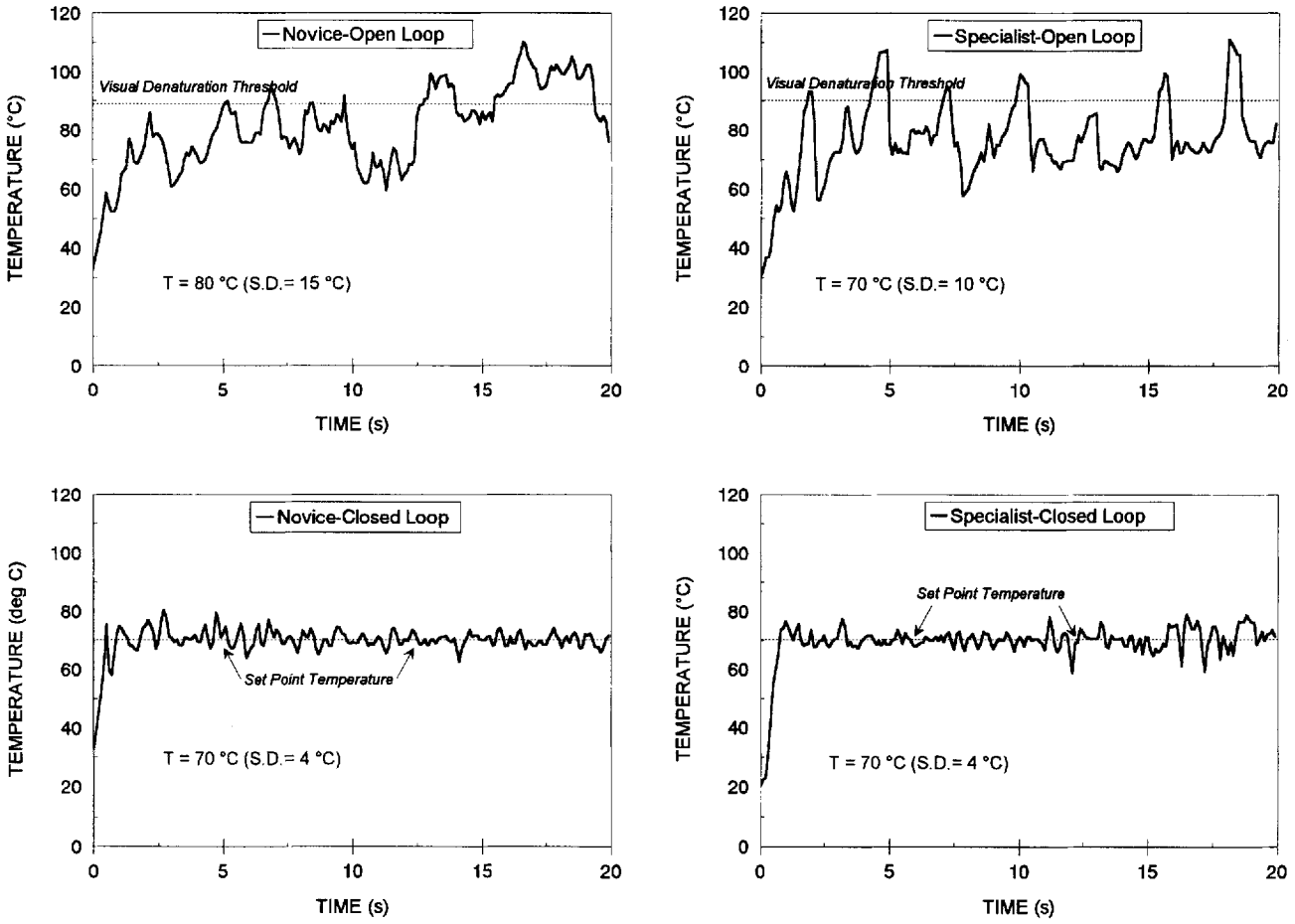

Fig. 2. Temperature profiles obtained during in vivo tissue welding. The laser repairs were completed using the conventional open loop method and with the TCPC system for a surgeon experienced (specialist-DPP) and untrained (novice-JMM) in tissue welding techniques.

sile strength of the repairs generally increased significantly with time for all of the temperature subgroups studies. This was also seen in the control repair, which was a simple suture closure (as described above). A notable exception to this trend was seen for the high temperature weld (95°C), which decreased slightly at 3 days when compared to the acute data. There was no significant difference between the tensile strengths for the chronic welds and the chronic suture controls. However, at 3 days, the welds made at 95°C were significantly weaker than the welds completed at 65°C ($P < 0.025$) or 75°C ($P < 0.05$).

Histopathological Findings

Gross examination immediately following repair demonstrated tissue blanching to occur ~2 mm across the repair (i.e., full width) in the low temperature groups (65°C and 75°C) and up to a width of 6 mm in the higher temperature groups (85°C and 95°C). In addition, the denatured tissue was bordered by a rim of erythema in the higher temperature groups. At 3 days postoperatively, the blanched tissue zones in the higher temperature repairs demonstrated poor cosmesis with areas of early tissue sloughing and a generally impaired healing response. This was not seen in wounds repaired at low temperatures. By postoperative day 8, tissue in the acute zone of blanching in the higher temperature welds continued to slough resulting in a shallow defect on either side of the repair. Gross observations made of the day 14 wounds were similar to the day 8 wounds in regard to the tissue defect for the higher temperature welds; however, all of the day 14 wounds showed nearly equivalent healing.

A photograph of the acute histology for laser repairs completed at 65°C and 95°C are given in

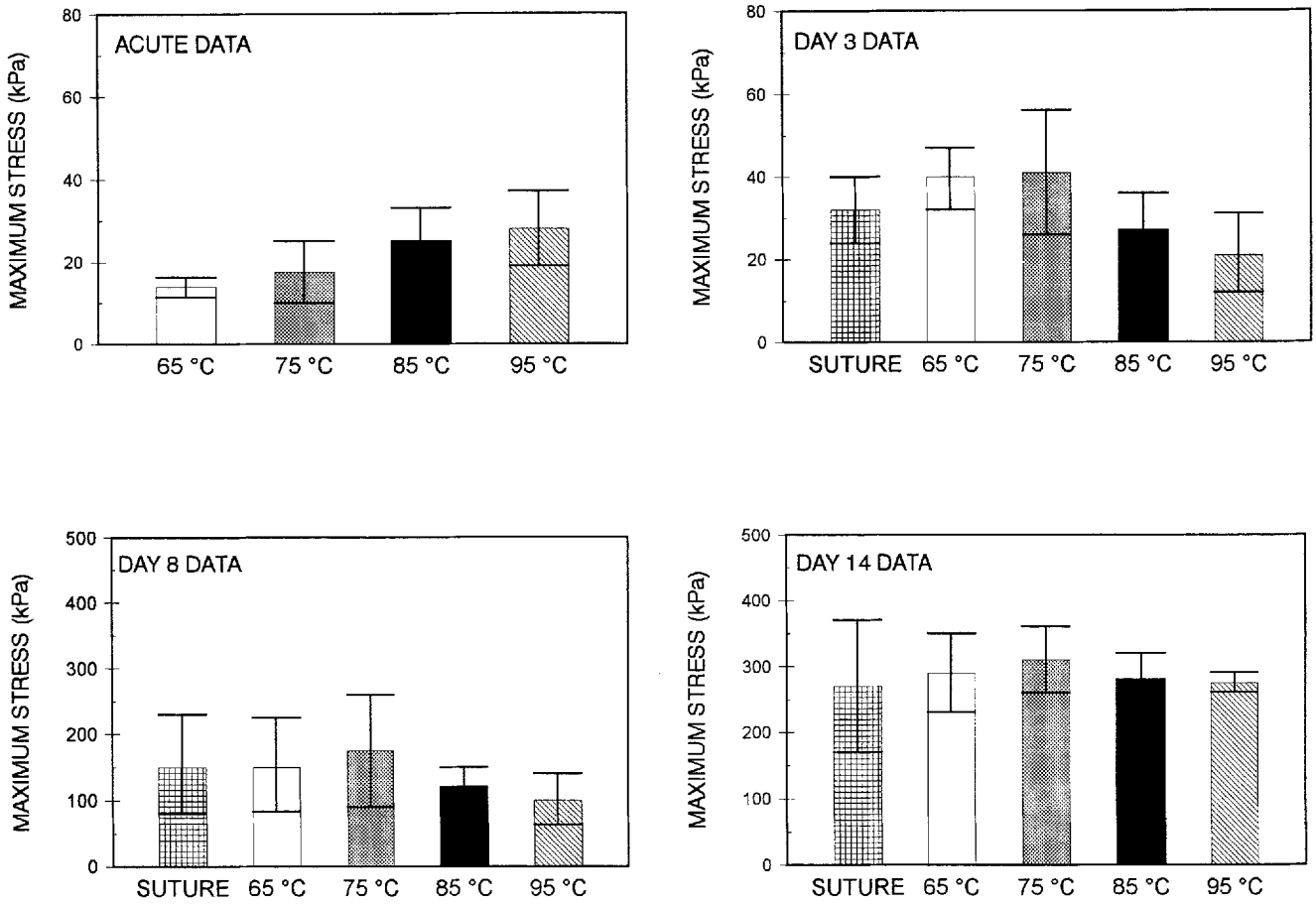

Fig. 3. Tensile strength measurements obtained for tissue welds completed using the TCPC system at several different temperatures. Strengths are shown for acute and chronic laser repairs.

Figure 4. Histologic analysis was performed on cross sections of each repair. For each temperature group, a quantitative determination of the thermally affected epithelium and denatured dermal collagen was calculated. The distance of the lateral thermal change observed in the epithelium and dermal collagen (from the center of the repair outward) was measured on each side of the repair. Epithelial thermal changes were defined by separation of the basal layer from the stratum spinosum and by stretching and polarization of the epithelial cell nuclei. Thermal damage to the dermal collagen was defined as a decrease in staining intensity and increase in homogeneous appearance of collagen fibers. The depth of these changes in the collagen were also measured (from the tissue surface into the bulk tissue).

The results of these measurements are given in Figure 5. The zone of lateral epithelial thermal change increased from an average of 1.2 mm in the 65°C group to 2.7 mm in the 95°C temperature group. Lateral thermal change in dermal collagen paralleled epithelial changes with an increase from 0.7 mm at 65°C to 2.3 mm at 95°C. The depth of collagen denaturation ranged from 2.6 mm at 65°C to 2.9 mm at 95°C. As expected, the width of thermal change was greatest near the tissue surface and became narrow deeper into the wound. In addition, the lateral thermal damage was somewhat asymmetric with the repaired incision (i.e., it varied from one side of the wound to the other) within the same specimen. This indicates that the accuracy of laser delivery affects the final histologic results. Consequently, the optimal weld may be achieved when the laser beam is aimed directly perpendicular to the wound so that equal energy can be delivered to both edges. Side to side movement of the laser should also be avoided during welding.

Histologic examination was also completed

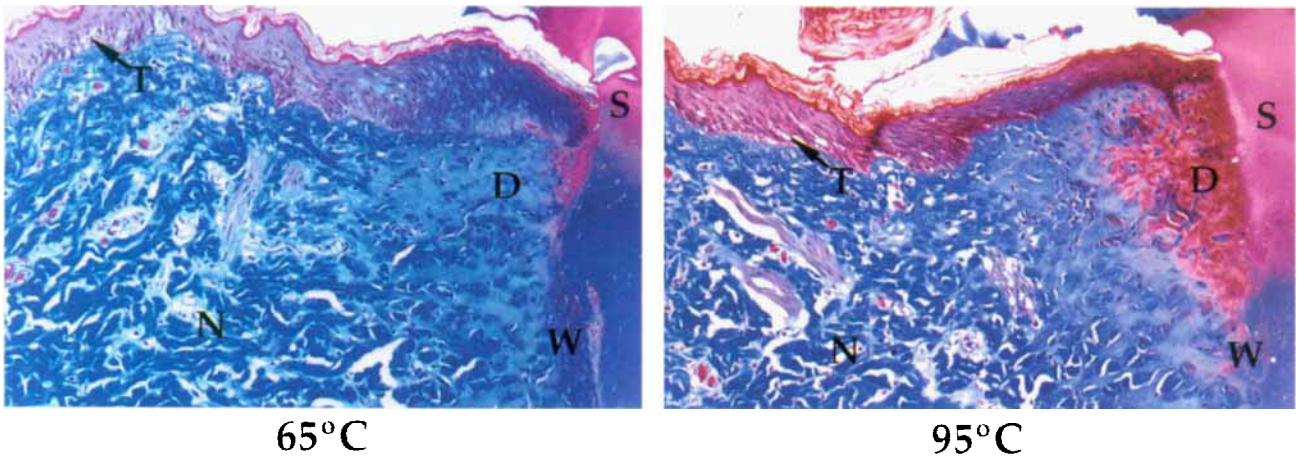

Fig. 4. Photographs of histologic specimens obtained from tissue repairs completed at 65°C and 95°C. Masson's Trichrome stain was used. The original magnification was 20×. Key: w = wound edge, d = denatured collagen, n = normal collagen, t = thermally changed epithelium, s = denatured solder.

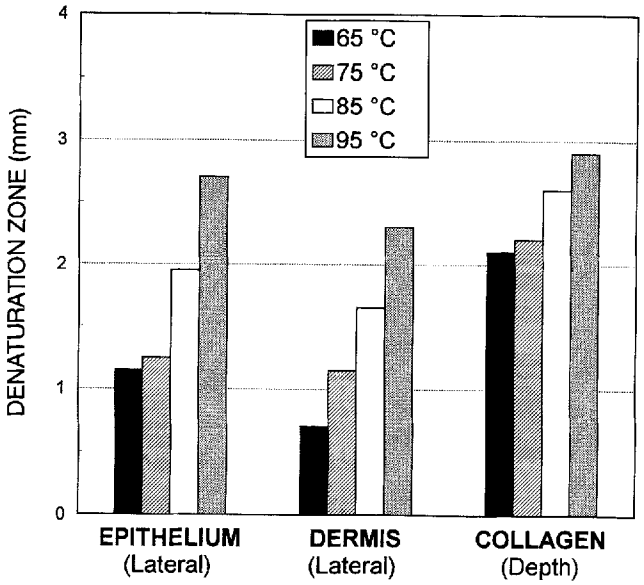

Fig. 5. The thermal denaturation zone measured from histologic examination of acute TCPC tissue welds. The value plotted for the lateral damage is the average distance for both sides of the repair, based on the criteria given in the text. The depth of collagen denaturation was determined via histological examination of a representative tissue section, as described in the text.

on the chronic repairs. All repairs at days 3 and 8 showed a marked increase in inflammatory cell infiltrate. The zone of thermal change maintained a similar pattern to the acute histology with marked remnants of thermal damage persisting in the 85°C and 95°C temperature groups at both day 3 and day 8. By day 14, the Trichrome stained repairs showed evidence of new collagen deposition in all wounds. Denatured albumin solder was also observed to be present in all wounds at day 14.

DISCUSSION

Lasers have been used for photocoagulation of soft tissue for >30 years. Heretofore, the primary mechanism to control the photocoagulation process has been visual feedback from changes occurring at the tissue surface. For debulking a large mass of soft tissues, this visual feedback mechanism has provided satisfactory results. However, the use of lasers for precise photocoagulation of soft tissue has been less successful. One of these precise procedures is the laser welding of tissues.

Although several groups have mastered tissue welding techniques for a variety of applications, the overall reproducibility for successful tissue welding repairs has been relatively low. The use of a real-time feedback control system to maintain a predetermined tissue temperature should increase the reliability of the laser welding procedure. Since tissue welding depends on the thermal denaturation of tissue proteins, the tissue temperature should provide a good indicator for such a feedback system to standardize the welding process.

These studies showed that a closed loop feedback control system could be used to maintain the temperature during a tissue welding procedure. The temperature controlled photocoagulation

(TCPC) system was capable of maintaining a predetermined temperature to ±4°C. This was significantly better than the open loop temperature control achieved by the specialist in laser welding techniques. The use of this closed loop system also demonstrated that the learning curve for generating stable tissue temperature profiles during tissue welding was short. The ease of use of the TCPC system should ultimately impact on the time necessary for training surgeons in tissue welding techniques.

As shown in Figure 2, the visual denaturation endpoint used by the specialist relied on the tissue exceeding 90°C. Following this visual cue, the specialist controls the weld process by redirecting the laser beam. The minimum response time of this human control system can be estimated as approximately 0.25 seconds (see Fig. 2). This response time is essentially limited by the specialist's reaction time and the latency period necessary for the visible tissue change to occur. Since this latency period is relatively short at 90°C (~5 ms) [5], the "open loop" response time is primarily due to the specialist's reaction time. Alternately, the response time of the TCPC system was limited by the thermopile detector to ~30 ms. The result of the differences between these two response times is shown in Figure 2. Nevertheless, it is noteworthy that the specialist was able to maintain a high degree of control around a temperature that should give a good clinical result. However, since the residence time for the laser beam on a given illuminated spot is ~1 second, it is clear from Figure 2 that portions of the weld were heated to high temperatures (>90°C) in the open loop model. These higher temperatures may lead to weaker welds in the short term (see chronic strength data above), which may decrease postoperative success.

Use of the closed loop TCPC system clearly demonstrated that tissue welds are sensitive to the weld temperature. The strength of acute laser welded repairs increased with increasing weld temperature. This is contrary to previous results, which indicate that a temperature of ~80°C produces optimal tissue welds [3,10]. This finding may be explained by the fact the primary strength in the weld is probably the result of tissue denaturation deep in the dermal layers. Based on the acute histology, the depth of thermal denaturation increased with temperature over the range studied (Fig. 5), which resulted in an increase in the weld "thickness." In addition, the depth of thermal damage was less than the total thickness of the tissue (>3.0 mm) for all of the temperatures studied. This indicates that a full-thickness weld was not obtained [8]. Consequently, the temperature achieved in the dermal layer during welding varied in depth and at deeper portions of the dermis was significantly less than the surface tissue temperature measured by the thermometer. Ultimately, TCPC of skin should be accomplished by monitoring the temperature at the weld within the dermal layer. This was not possible for the TCPC system used here, because of the short penetration depth for light at the infrared wavelengths *monitored*. Alternatively, a laser at a different wavelength, such as the near infrared wavelengths ~800 nm [13], where the absorption depth is significantly greater, would allow the laser energy to be more evenly distributed across the weld (i.e., efficiently coupled into the inner dermal layers). In this case, the temperature gradient across the tissue should be less, thus the surface temperature will more closely match the bulk tissue temperature [10].

The TCPC studies also clearly demonstrated that the chronic healing of the laser weld was highly dependent on the temperature achieved during the repair. This is extremely significant for procedures where the cosmesis is important. Furthermore, the chronic tensile strength measurements showed that the healing response to excessive temperatures also affects the short term strength of the repair. This is shown in the day 3 data, where the 85°C and 95°C temperature groups had the lowest tensile strength measurements. This decrease in tensile strength can be correlated to the histologic findings, which showed marked increases in the acute damage to surrounding tissue (Fig. 5), lateral to the welded tissue. The chronic result of this acute damage was sloughing of tissue bordering the repair, which resulted in a *decrease* in the functional thickness of the tissue. This healing response to excessive damage ultimately affects all tissue welding procedures and may explain the short-term *decrease* in the strength of tissue welds reported by others [14]. It is noteworthy that this deleterious "subchronic" effect was not seen for the TCPC tissue welds completed at lower temperatures. Thus the use TCPC systems should enhance the reproducibility and ultimately the success in tissue welding with the proper choice of welding temperature.

The final outcome of laser photocoagulation procedures is dependent on the acute thermal injury and the healing response of the damaged tis-

sue. The acute thermal damage may be understood based strictly in terms of denaturation of proteins vis-a-vis the absorption of laser energy followed by the thermal transport of heat into the surrounding tissue. The healing process, in contrast, is dependent on several factors, including the effect of elevated temperature on cell survivability, and the thermal stability of the biochemical elements involved in the acute phase of wound healing, including the endogenous growth factors mediating tissue repair. The TCPC system is currently being used in further studies to better understand important aspects of wound healing following laser photocoagulation procedures.

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